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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/580,035	BIGNON ET AL.	
	Examiner	Art Unit	
	Cherie M. Woodward	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 May 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-40* is/are pending in the application.

4a) Of the above claim(s) *1,2,8,16 and 27-34* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *3-7,9-15,17-26,and 35-40* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Formal Matters

1. Applicant's Response filed 5/19/2009 are acknowledged and entered. Claims 1-40 are pending. claims 1, 2, 8, 16, and 27-34 are withdrawn as being drawn to non-elected inventions. Claims 3-7, 9-15, 17-26, and 35-40 are under examination as they are drawn to the species of Formula I.

Response to Arguments

Objections/Rejections Withdrawn

2. The rejection of claims 3-7, 9-15, 18-22, 24-26, and 35-40 under 35 U.S.C. 102(b) as being anticipated by Huille et al., WO 00/30618 (published 2 June 2000) (cited on Applicant's IDS of 9/21/2006) (the English language translation of which is US Patent 6,630,171) (see Patent family history for WO 00/30618, last accessed 11/28/2008), as evidenced by the Handbook of Chemistry and Physics, 88th Ed. 2008, (Viscosities of Liquids, Section 6, pages 175-179) and Akiyoshi, et al., (J Controlled Release. 1998;54:313-320), is withdrawn.

3. The provisional rejection of claim 3-7, 9-15, 17, and 21-26 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 4-11, 13-18, 22, 23, and 29 of copending Application No. 11/808,456, is withdrawn.

4. The provisional rejection of claims 3-7, 9-15, 17, and 21-26 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-7, 10-18, and 25-36 of copending Application No. 11/878947, is withdrawn.

5. The provisional rejection of claims 3-7, 9-15, 17, 16-26, and 35-40 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-24 and 26 of copending Application No. 10/516,733, is withdrawn.

Objections/Rejections Maintained

Claim Rejections - 35 USC § 112, Second Paragraph

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claim 7 remains rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Applicant argues the examiner is "mistaken and confused" as to the chemical identities of the recited compounds (Remarks, pp. 13-14). Applicant argues that polyethylenimine is a separate chemical entity to the genus of "organic cations based on polyamine" (Remarks, p. 14). Applicant argues that the recitation in claim 7 is a proper Markush Group and that no "such as" language is used (Remarks, p. 14).

Applicant's arguments have been fully considered, but they are not persuasive. The indefiniteness rejection was not based on an improper Markush Group nor does the Markush group contain "such as" language. *Ex parte Wu* was cited as an example of a related similar situation for Applicant's benefit.

In response to Applicant's arguments regarding the genus of polyamines and polyethylenimine, the examiner fully understands the structural and functional difference of polyamines and polyethylenimines (PEIs). However, the claim is not drawn to "polyamines", but rather to "organic cations based on polyamines" [emphasis added]. It is unclear whether the "based on" language encompasses only organic cations comprising only primary amines or whether it can include organic cations containing secondary amines (*i.e.* branched PEIs, which contain primary, secondary, and tertiary amino groups). Further, the "based on" language used throughout the Markush group is indefinite, as there are no structural limitations as to what the "based on" may represent structurally or functionally. Moreover, as another example of narrow and broad limitations within the same claim, the Markush group recites "organic cations based on amino acids" and also recites "organic cations based on lysine" (lysine is a species of amino acid), "organic cations based on arginine" (arginine is a species of amino acid).

Applicant is also referred to *Ex parte Miyazaki* (BPAI 11/19/2008) (Horner, APJ) (precedential). A five member expanded panel of the Board held that "if a claim is amenable to two or more plausible claim constructions, the USPTO is justified in requiring applicant to more precisely define the metes and bounds of the claimed invention by holding the claim unpatentable under 35 USC 112, second paragraph, as indefinite." *Mizayzaki*, slip op. at 11-12.

8. Claim 24 remains rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Applicant argues that claim 24 sets forth a Markush group not a broad or narrow range (Remarks, p. 14). Applicant argues that the examiner is "again...mistaken and confused" as to the claiming elements

of a Markush group (Remarks, p. 14). Applicant argues that the recitation in claim 24 is a proper Markush Group and that no "such as" language is used (Remarks, p. 14).

Applicant's arguments have been fully considered, but they are not persuasive. The indefiniteness rejection was not based on an improper Markush Group nor does the Markush group contain "such as" language. *Ex parte Wu* was cited as an example of a related similar situation for Applicant's benefit. Broad and narrow genera/subgenera/species within the same claim, whether or not they are in a Markush group, are indefinite. The fact that a claim contains a Markush group does not negate the indefiniteness of a genera, subgenera, and species listed among alternatives in the same claim where the metes and bounds of the genera, subgenera, and species are unclear. See MPEP § 2173.05.

Claim 24 contains a broad recitation of "proteins" followed by alternative narrow recitations of specific proteins (i.e. albumins, interferons, cytokines, antibodies, etc). The broad recitation of proteins and the narrower recitations of subgeneras and species of proteins render the metes and bounds of the claim unclear and indefinite.

Applicant is also referred to *Ex parte Miyazaki* (BPAI 11/19/2008) (Horner, APJ) (precedential). A five member expanded panel of the Board held that "if a claim is amenable to two or more plausible claim constructions, the USPTO is justified in requiring applicant to more precisely define the metes and bounds of the claimed invention by holding the claim unpatentable under 35 USC 112, second paragraph, as indefinite." *Mizayzaki*, slip op. at 11-12.

Claim Rejections - 35 USC § 112, First Paragraph

Scope of Enablement

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 3-7, 9-15, 17-26, and 35-40 remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an IL-2 formulation comprising a polyglutamate polymer grafted with α-tocopherol which spontaneously associates with bovine serum albumin to form a gel *in vitro* and *in vivo* in a concentration-dependent manner, does not reasonably provide enablement for the claimed super genus of structural variants comprising at least one active principle (AP) and a biodegradable polymer (PO) carrying hydrophobic groups (HG) or the super-genus of biodegradable polymers of Formula I, for the reasons of record and the reasons set forth herein.

Applicant argues that the specification discloses examples of polymers with different hydrophobic groups exemplified by cholesterol and n-dodecanol and that one of skill in the art would understand how to manufacture different polymers and how to associate active principles with these polymers (Remarks, p. 16). Applicant argues that any experimentation required would be routine and not undue (Remarks, p. 16). Applicant argues that the skilled artisan could make the claimed invention and test to determine whether the polymers and formulations have the requisite properties (Remarks, pp. 16-17).

Applicant's arguments have been fully considered, but they are not persuasive. The rejection stated that the specification does not reasonably provide enablement for the claimed super genus of structural variants comprising at least one active principle (AP) and a biodegradable polymer (PO) carrying hydrophobic groups (HG) or the super-genus of biodegradable polymers of Formula I. Examples of two hydrophobic groups (i.e. cholesterol and n-dodecanol) alone are insufficient to provide enabling support for the numerous genera of structural variants comprising at least one AP and a PO or the generas of biodegradable polymers.

As explained of record, the only active principle (AP) recited in the claims is "an interleukin" (see claims 3-7, 9, 10, 19-26, and 35-40). The examples in the specification for active principles on page 23 are non-specific, generic generas, including "proteins." Claim 7 is a generic formula with numerous alternative structures. Claim 9 recites a generic structure for the hydrophobic group (HG), but does not otherwise limit the other structural variables of Formula I. The structure of Formula I in claim 9 is very basic and there are insufficient variable moieties to account for the full structure of a sufficient number of representative species of Formula I. It is noted that in claim 7 "m" can be zero and in claim 9 "l" can be zero. Based on the structural information in claims 7, 9, and 10, it appears that the biodegradable polymer comprise C6-C30 esters of polyaspartic or polyglutamic acid. There is insufficient structural information in the claims or the specification to provide an adequate description of discrete species of the claimed biodegradable polymers. Claim 11 recites subgenera of hydrophobic groups, but does not otherwise limit the hydrophobic groups to any particular species. Claims 7 and 12-14 are silent as to the structural requirements for the hydrophobic group. Claim 15 does not limit the number of hydrophobic groups in the aspartic or glutamic unit polymers. Claims 17 and 18 limit the hydrophobic radical R6 to cholesterol or a derivative of a tocopherol, but the claims still only describe sub-generas and not discrete structural species. The generas of polymers (PO) in claim 21 do not really limit the structure of the formulation when the polymers can be any polyamino acids, polysaccharides, chitosans, mucopolysaccharides, gelatins, and mixtures thereof. Claim 23 limits the interleukin to interleukin-2, but claim 3, from which

claim 23 depends, recites "at least one active principle" and claim 23 does not further limit other interleukins or active principles that may comprise the composition. Claim 24 recites that the formulation further comprises at least one active principle selected from super-generas that include proteins, glycoproteins, a PEG, a polysaccharide, a liposaccharide, a polynucleotide, an oligonucleotide, a peptide, and it also recites more narrow examples of peptides and mixtures thereof. Claims 19, 20, 22, 25, 26, and 35-40 do not adequately limit the structure of the polymer or active principle at all. The specification discloses a subgenera comprising an IL-2 formulation comprising polyglutamate grafted with α-tocopherol which spontaneously associates with bovine serum albumin to form a gel *in vitro* and *in vivo* in a concentration-dependent manner (Examples 1-8; specification pp. 25-30). However, no other representative structures of Formula I or the generic structure of an active principle and a biodegradable polymer are sufficiently taught in the specification.

The suggestion of Applicant's representative that a skilled artisan make and test any generic number of the generic formulations is tantamount to an invitation to experiment. See *Enzo Biochem, Inc. v. Calgene, Inc.*, 188 F.3d 1362, 52 USPQ2d 1129 (Fed. Cir. 1999). Such an invitation does not constitute an enabling disclosure.

The determination of whether Applicant has met his burden of disclosing how to make and use the invention to the public in order to satisfy the *quid pro quo* requirement of disclosure in exchange for a patent has not been adequately met by the instant claims or specification. From the early days of the republic, our patent law has required that in exchange for a government-sanctioned monopoly on the rights to an invention or discovery, the inventor must teach the world the secret behind the method or device. Compare 35 USC § 112 (1984) with Act of April 10, 1790, ch. 7, § 2, 1 Stat. 109 ("specification shall be so particular . . . as not only to distinguish the invention or discovery from other things before known and used, but also to enable a workman or other person skilled in the art of manufacture . . . to make, construct or use the same, to the end that the public may have the full benefit thereof, after the expiration of the patent term"); see also, *Bonito Boats, Inc. v. Thunder Craft Boats, Inc.*, 489 U.S. 141, 146-51, 103 L. Ed. 2d 118, 109 S. Ct. 971 (1989); *In re Goodman*, 11 F.3d 1046, 1050 (Fed. Cir. 1993) (specification must teach how to make and use the invention as broadly as it is claimed). The rationale for the enablement requirement is that an inventor deprives the public of nothing which it enjoyed before his discovery, but gives something of value to the community by adding to the sum of human knowledge. He may keep his invention secret and reap its fruits indefinitely. In consideration of its disclosure and the consequent benefit to the community, the patent is granted. *United States v. Dubilier Condenser Corp.*, 289 U.S. 178, 186-87, 77 L. Ed. 1114, 53 S. Ct. 554 (1933) (citations omitted); see also *O'Reilly v. Morse*,

56 U.S. 62, 119-20, 14 L. Ed. 601, (15 How. 62, 127-28) (1853) (Taney, C.J.) (one skilled in the art must be able to produce precisely the described result by using the means specified by the inventor); *Grant v. Raymond*, 31 U.S. 217, 247 (31 Peters 141, 160) (1832) (Marshall, C.J.) (correct specification is a prerequisite to obtaining a patent in order to give the public "the advantage for which the privilege is allowed, and is the foundation of the power to issue the patent."). When a putative inventor fails or refuses to fulfill the obligation to teach precisely what is claimed, the inventor is not entitled to the protections of the patent law. See, e.g., *Morton Int'l, Inc. v. Cardinal Chem. Co.,* 5 F.3d 1464, 1469-70 (Fed. Cir. 1993) (affirming determination of lack of enablement where fifty examples in specification "obviously teach something," but not what was defined in the claims).

The grant of a patent is premised on this fundamental bargained-for exchange. The inventor must provide a full, complete, and enabling description of the invention and, in exchange, the government provides the inventor with the right to exclude others from practicing the invention. See *LizardTech, Inc., v. Earth Res. Mapping, Inc.*, 424 F.3d 1336, 1344 (Fed. Cir. 2005) (describing enablement as an essential part of the patent bargain); in *Liebel-Flarsheim Co., v. Medrad.*, Inc, (*Liebel II*) 481 F.3d 1371 (Fed. Cir. 2007) (holding that the claims must enabled the full scope of the broadest claim, even if one or more embodiments are specifically enabled) (at p. 14, last paragraph to page 15, first paragraph of CAFC slip op. 06-1156, 22 March 2007); and *AK Steel Corp v. Sollac and Ugine*, 344 F.3d 1234, 1343-44 (Fed. Cir. 2003). Moreover, the CAFC has held that claims broad enough to encompass significant nonenabled subject matter will be found nonenabled (*Sitrick v. Dreamworks*, LLC, 516 F.3d 993 (Fed. Cir. 2008). The holding in *Sitrick* is a restatement of the precedential CCPA holding in *In re Cook and Merigold*, 169 USPQ 298 (CCPA 1971) (holding that broad claims may be rejected merely because they read on a significant number of inoperative species when examiner sets forth reasonable grounds in support of his or her conclusions that the claims may read upon inoperative subject matter and it becomes incumbent upon applicant either to reasonably limit claims where operativeness has not been challenged or to rebut examiner's challenge by submission of representative evidence or by persuasive arguments based on known laws of physics and chemistry).

Due to the large quantity of experimentation necessary to determine how to make or use the claimed methods without resorting to undue experimentation to determine the structure of the composition or how to use it *in vitro* or *in vivo*, the lack of direction/guidance presented in the specification regarding same, the absence of sufficient working examples directed to same, the complex nature of the invention, the state of the prior art establishing that specific polyglutamate block and co-block polymers are known, but not the super-genera of polymer structures claimed by Applicant, and the

breadth of the claims which fail to recite a specific structure or use for the specific structure, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

Claim Rejections - 35 USC § 112, First Paragraph

Written Description

11. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

12. Claims 3-7, 9-15, 17-26, and 35-40 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement, for the reasons of record and the reasons set forth herein.

Applicant argues that the specification discloses the chemical structure of polymers encompassed by the claimed invention and the physical properties and functional characteristics of the polymers (Remarks, p. 18). Applicant argues that the specification disclose that the polymers encompassed by the claimed invention can associate spontaneously with active principles and that the active principles are listed on page 23 (Remarks, p. 18). Applicant argues that the specification discloses examples of polymers with different hydrophobic groups and that are associated with different active principles (Remarks, p. 18). Applicant argues that the skilled artisan would understand from the disclosure of "representative examples" that Applicant was in possession of the common attributes of the elements possessed by the members of the genus in view of the species disclosed (Remarks, p. 18).

Applicant's argument has been fully considered, but it is not persuasive. As stated of record, the claims are drawn to a super-genus of potential structures which are not adequately described in the specification in such a way that one of ordinary skill in the art would be aware that Applicant was in possession of the full scope of the claimed genus. For example, the only active principle (AP) recited in the claims is "an interleukin" (see claims 3-7, 9, 10, 19-26, and 35-40). Contrary to Applicant's argument, the examples in the specification for active principles on page 23 are non-specific, generic generas, including "proteins." Claim 7 is a generic formula with numerous alternative structures. Claim 9 recites a generic structure for the hydrophobic group (HG), but does not otherwise limit the other structural variables of Formula I. The structure of Formula I in claim 9 is very basic and there are insufficient variable moieties to account for the full structure of a sufficient number of representative species of Formula I. It is noted that in claim 7 "m" can be zero and in claim 9 "I" can be zero. Claim 7

is also silent as to the structural requirements for the hydrophobic group. Based on the structural information in claims 7, 9, and 10, it appears that the biodegradable polymer comprise C6-C30 esters of polyaspartic or polyglutamic acid. There is insufficient structural information in the claims or the specification to provide an adequate description of discrete species of the claimed biodegradable polymers. Claim 11 recites subgenera of hydrophobic groups, but does not otherwise limit the hydrophobic groups to any particular species. Claims 7 and 12-14 are silent as to the structural requirements for the hydrophobic group. Claim 15 does not limit the number of hydrophobic groups in the aspartic or glutamic unit polymers. Claims 17 and 18 limit the hydrophobic radical R6 to cholesterol or a derivative of a tocopherol, but the claims still only describe sub-generas and not discrete structural species. The generas of polymers (PO) in claim 21 do not really limit the structure of the formulation when the polymers can be any polyamino acids, polysaccharides, chitosans, mucopolysaccharides, gelatins, and mixtures thereof. Claim 23 limits the interleukin to interleukin-2, but claim 3, from which claim 23 depends, recites "at least one active principle" and claim 23 does not further limit other interleukins or active principles that may comprise the composition. Claim 24 recites that the formulation further comprises at least one active principle selected from super-generas that include proteins, glycoproteins, a PEG, a polysaccharide, a liposaccharide, a polynucleotide, an oligonucleotide, a peptide, and it also recites more narrow examples of peptides and mixtures thereof. Claims 19, 20, 22, 25, 26, and 35-40 do not adequately limit the structure of the polymer or active principle at all.

While "examples explicitly covering the full scope of the claim language" typically will not be required, a sufficient number of representative species must be included to "demonstrate that the patentee possessed the full scope of the [claimed] invention." *Lizardtech v. Earth Resource Mapping, Inc.*, 424 F.3d 1336, 1345, 76 USPQ2d 1724, 1732 (Fed. Cir. 2005). In the instant case, the generic recitation of some structural components without the disclosure of a sufficient number of fully formed structural species, cannot demonstrate a sufficient number of representative species.

Possession may not be shown by merely describing how to obtain possession of members of the claimed genus or how to identify their common structural features (see, *Univ. of Rochester v. G.D. Searle & Co.*, 358 F.3d 916, 927, 69 USPQ2d 1886, 1895 (Fed. Cir. 2004); accord *Ex Parte Kubin*, 2007-0819, BPAI 31 May 2007, opinion at p. 16, paragraph 1). The specification does not clearly allow persons of ordinary skill in the art to recognize that he or she invented what is claimed (see *Vas-Cath* at page 1116).

Conception does not occur unless one has a mental picture of the structure of the chemical, or is able to define it by its method of preparation, its physical or chemical properties, or whatever characteristics sufficiently distinguish it. *Amgen Inc. v. Chugai Pharmaceutical Co.,* 927 F.2d 1200, at

1206, 18 USPQ2d 1016, at 1021 (Fed. Cir. 1991). In such instances the alleged conception fails not merely because the field is unpredictable or because of the general uncertainty surrounding experimental sciences, but because the conception is incomplete due to factual uncertainty that undermines the specificity of the inventor's idea of the invention. *Burroughs Wellcome Co. v. Barr Laboratories Inc.*, 40 F.3d 1223, 1229, 32 USPQ2d 1915, 1920 (Fed. Cir. 1994). Reduction to practice in effect provides the only evidence to corroborate conception (and therefore possession) of the invention. *Id.*

Applicant is also referred to *Ariad Pharmaceuticals Inc. et al., v. Eli Lilly and Co.*, Slip Op. 2008-1248 (Fed. Cir. 3 April 2009), especially at p.7, stating that "the written description requirement is not satisfied by the appearance of mere indistinct words in a specification or a claim, even an original claim…A description of what a material does, rather than of what it is, usually does not suffice" quoting *Enzo Biochem Inc., v. Gen-Probe Inc.*, 323 F. 3d 956, 968 (citing *Regents of the Univ. of Cal. v. Eli Lilly*, 119 F.3d 1159, 1568 (Fed. Cir. 1997) and *Univ. of Rochester v. G.D. Searle & Co*, 358 F3d. 916, 926 (Fed. Cir. 2005). In *Ariad*, the Court held that to satisfy the written description requirement for the asserted claims, the specification must demonstrate that Applicant possessed the claimed methods by sufficiently disclosing the structure of the molecules capable of performing the disclosed function, citing *Capon v. Eshhar*, 418 F.3d 1349,1357 (Fed. Cir. 2005) (*Ariad*, Slip Op. at 10).

The concerns raised by the examiner specifically relate to aspects of Applicant's generic invention which are not adequately described. Applicant is encouraged to review the recent decision in *Carnegie Mellon University et al., v. Hoffman-La Roche, Inc.,* et al., Slip Op. 2007-1266 (Fed. Cir., 8 September 2008), where the CAFC specifically addressed the issue of generic claims to biological and chemical subject matter. The Court stated that "[t]he basic function of a patent specification is to disclose an invention. It has long been the case that a patentee can lawfully claim only what he has invented and described, and if he claims more his patent is void'" (citing *O'Reilly v. Morse*, 56 US (15 How.) 62, 121 (1853)) (Slip Op., at 10). "The written description serves a *quid pro quo* function 'in which the public is given 'meaningful disclosure in exchange for being excluded from practicing the invention for a limited period of time'" (citing *Univ. of Rochester v. G.D. Searle & Co.*, 358 F.3d 916, 69 USPQ2d 1886 (Fed. Cir. 2004), quoting *Enzo Biochem, Inc. v. Gen-Probe Inc.*, 323 F3d 956, 970 (Fed. Cir. 2002) (Slip Op., at 10). The *Carnegie Mellon* Court held that "[o]ne must show that one has possession, as described in the application, of sufficient species to show that he or she invented and disclosed the totality of the genus" (Slip Op., at 18).

In the absence of sufficient recitation of distinguishing characteristics, the specification does not provide adequate written description of the claimed genus, which is a liquid formulation comprising at

least one active principle (AP) which is an interleukin and a biodegradable polymer (PO) carrying hydrophobic groups (HG). One of skill in the art would not recognize from the disclosure that the applicant was in possession of the genus.

Claim Rejections - 35 USC § 103

13. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

14. Claims 3-7, 9-15, 17-26, and 35-40 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Huille et al., WO 00/30618 (published 2 June 2000) (cited on Applicant's IDS of 9/21/2006) (the English language translation of which is US Patent 6,630,171) (see Patent family history for WO 00/30618, last accessed 11/28/2008), Lambert et al., US Patent 7,030,155 (benefit to 5 June 1998), and Singh et al., US Patent 5,102,872 (7 April 1992), as evidenced by the Handbook of Chemistry and Physics, 88th Ed., 2008 (Viscosities of Liquids, Section 6, pages 175-179) and Akiyoshi, et al., (J Controlled Release. 1998;54:313-320), for the reasons of record and the reasons set forth herein.

Applicant argues that the '618 publication/'171 patent does not disclose a gelled deposit or solution comprising 30 mg/ml of bovine serum albumin and that the combination of the other references does not cure this deficiency (Remarks, pp. 23-24). Applicant argues that the level of skill in the art has not been resolved (Remarks, p. 24). Applicant argues that the examiner has not set forth any support under the rationales for obviousness (Remarks, pp. 24-25).

Applicant's arguments have been fully considered, but they are not persuasive. The '618 publication/'171 patent teaches a solution of 0.5% BSA, but does not specifically recite a concentration of 30 mg/ml. The '872 patent teaches compositions comprising IL-2 conjugated to a polyol in order to approve the solubility of IL-2 in a sustained release formulation (column 3, lines 6 and 49, and column 5, lines 34-41). The addition of human or bovine serum albumin is taught as stabilizing and modulating the release of the polyol-IL-2 from polymer microcapsules (column 5, lines 59-65). The '872 patent teaches that precise quantity of serum albumin will vary, but will generally be within the ratio range of about 1:5 to about 1:30 IL-2-to-serum albumin by weight (column 5, lines 59-68 to column 6, lines 1-5). This weight ratio is within the recited 30 mg/ml. Alternatively, based on the teachings of both the '872 patent and the '618 publication/'171 patent, it would be obvious to optimize the concentration of the BSA.

Generally, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955).

Regarding Applicant's assertion that the level of skill in the art has not been resolved, Applicant's argument is not well founded. The level of skill in the art is readily discernable from the authors and inventors of the disclosed prior art references. One need not have a PhD with multiple years of postdoctoral experience to understand basic polymer chemistry. In unpredictable arts, the level of skill is generally high. However, in fields of endeavor with a dearth of prior art, the level of skill need not be as high. Moreover, because the level of skill is readily discernable from the prior art references themselves, the examiner need not waste Applicant's time or resources reciting facts that are readily apparent or easily discernable.

Regarding Applicant's argument that the examiner has not set forth any support under the enumerated rationales, Applicant's attention is drawn to the finds of fact and discussion by the examiner in the Office Action mailed 12/3/2008, specifically pages 15-16. The examiner is not required to identify rationales by name or number. As plainly stated of record, a person of ordinary skill in the art at the time the invention was made would have reasonably known that hydrophobic groups could be grafted to proteins, as taught by the '155 patent. Further, a person of ordinary skill in the art would have been able to make hydrophobic moieties grafted to proteins or amino acid polymers by using well-known methodologies and protocols, such as the ones taught by the '155 patent, and the resulting structure and function of the grafted hydrophobic group would have been predictable; to improve solubility of poorly soluble drugs. Additionally, a person of ordinary skill in the art at the time the invention was made would have reasonably known that IL-2 mediates a successful immune response to antigens, as taught by the '872 patent (column 2, lines 31-32). Moreover, a person of ordinary skill in the art would have known that attaching a polyol to IL-2 would increase its half-life and improve its solubility in a sustained release formulation, as taught by the '872 patent.

It would have been obvious and predictable to merely substitute a tocopherol derivative, such as the vitamin E (α-tocopherol) with the cholesterol taught by the '618 publication because the '155 patent teaches the addition of hydrophobic moieties to proteins in order to improve the solubility of poorly soluble drugs and the '618 publication teaches cholesterol grafted to polyglutamate block polymers for the same purpose. Both the level of skill in the art in the field of molecular biology and the actual

construction of cholesterol and tocopherol derivative grafts to proteins, as taught by the '618 publication and the '155 patent, make the substitution predictable. With regard to the gel-forming properties of the claimed composition, the rheological properties of gel formation are inherent physical properties of the composition. For example, compositions comprising polymers carrying hydrophobic groups will spontaneously disassociate proteins from the polymer complex in the presence of bovine serum albumin, as evidenced by Akiyoshi, et al., (especially at p. 318, column 2, last paragraph to p. 319, column 1, first paragraph, and p. 319, column 2, last paragraph).

With regard to the question of Applicant's representative with regard to the examiner's statement as to the viscosity of water, the examiner was not intimating that Applicant was claiming water, rather she was merely stating a physical fact that the viscosity of water meets the viscosity limitations in instant claims 3, 5, and 20, as evidenced by the Handbook of Chemistry and Physics (Viscosities of Liquids) (Section 6, pages 175-179).

Applicant has not provided any data or evidence to rebut the examiner's assertion that claim 22 is amenable to testing. Because the Patent Office does not have the facilities to determine whether the formulation of claim 3 (as taught by the '618 publication) has a % weight fraction of interleukin(s) not associated with submicronic particles of ≤ 1, the burden is on the application to show a novel and unobvious difference between the claimed scaffold and that of the prior art. See *In re Brown*, 59 CCPA 1036, 459 F.2d. 531, 173 USPQ 685 (CCPA 1972) (holding at 1041, "[a]s a practical matter, the Patent Office is not equipped to manufacture products by the myriad of processes put before it and then obtain prior art products and make physical comparisons therewith") and *Ex parte Gray*, 10 USPQ 2d 1922, 1924-25 (PTO Bd. Pat. App. & Int.).

Obviousness-Type Double Patenting Rejections

15. Claims 3-7, 9-15, 18-22, 24, and 36-40 remain rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-35 of U.S. Patent No. 6,630,171 (7 October 2003) as evidenced by the Handbook of Chemistry and Physics (Viscosities of Liquids, Section 6, pages 175-179) and Akiyoshi, et al., (J Controlled Release. 1998;54(313-320), and Singh et al., US Patent 5,102,872 (7 April 1992) (previously cited of record), for the reasons of record and the reason set forth herein.

Applicant argues that the '171 patent does not disclose a gelled deposit or solution comprising 30 mg/ml of bovine serum albumin and that the combination of the other evidentiary references do not cure this deficiency (Remarks, p. 26).

Applicant's argument has been fully considered, but it is not persuasive. The '171 patent teaches a solution of 0.5% BSA, but does not specifically recite a concentration of 30 mg/ml. However, in response to Applicant's argument, Applicant's attention is also drawn to the '872 patent, previously cited of record and discussed at length of record and above. The '872 patent, teaches compositions comprising IL-2 conjugated to a polyol in order to approve the solubility of IL-2 in a sustained release formulation (column 3, lines 6 and 49, and column 5, lines 34-41). The addition of human or bovine serum albumin is taught as stabilizing and modulating the release of the polyol-IL-2 from polymer microcapsules (column 5, lines 59-65). The '872 patent teaches that precise quantity of serum albumin will vary, but will generally be within the ratio range of about 1:5 to about 1:30 IL-2-to-serum albumin by weight (column 5, lines 59-68 to column 6, lines 1-5). This weight ratio is within the recited 30 mg/ml.

Alternatively, based on the teachings of both the '872 patent and the '171 patent, it would be obvious to optimize the concentration of the BSA. Generally, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955). Applicant is also referred to *In re Baselle Poliolefine Italia*, 2007-1450, slip op. at 13 (Fed. Cir. 13 Nov 2008).

16. Claims 3-7, 9-15, 17, and 21-26 remain provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 3-7, 9-15, and 21-26 of copending Application No. 10/580023, for the reasons of record and the reasons set forth herein.

Applicant states that a terminal disclaimer has been filed with the response on 5/19/2009 (Remarks, p. 26). However, no terminal disclaimer was filed. Accordingly the rejection is maintained.

17. Claims 3-7, 9-15, 17, 21, 22, and 24-26 remain provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 3-7, 9-15, and 21-26 of copending Application No. 10/580037, for the reasons of record and the reasons set forth herein.

Applicant states that a terminal disclaimer has been filed with the response on 5/19/2009 (Remarks, p. 26). However, no terminal disclaimer was filed. Accordingly the rejection is maintained.

Conclusion

NO CLAIM IS ALLOWED.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to CHERIE M. WOODWARD whose telephone number is (571)272-3329. The examiner can normally be reached on Monday - Friday 9:30am-6:00pm (EST).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Manjunath N. Rao can be reached on (571) 272-0939. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Cherie M. Woodward/
Primary Examiner, Art Unit 1647